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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/700,291 | 11/03/2003 | David J. Wasilko | PC23192A | 6793 |

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PFIZER INC.
PATENT DEPARTMENT, MS8260-1611
EASTERN POINT ROAD
GROTON, CT 06340

| EXAMINER | |
|---|---|
| CHEN, STACY BROWN | |
| **ART UNIT** | **PAPER NUMBER** |
| 1648 | |

DATE MAILED: 01/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/700,291 | WASILKO ET AL. | |
| | Examiner | Art Unit | |
| | Stacy B. Chen | 1648 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *17 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-5 and 7-83* is/are pending in the application.

4a) Of the above claim(s) *32-36 and 56-83* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-31 and 37-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *August 12, 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

1. Applicant's amendment filed October 17, 2005 is acknowledged and entered. Claims 1-5 and 7-83 are pending. Claims 1-5, 7-31 and 37-55 are under examination. Claims 32-36 and 56-83 remain withdrawn from consideration being drawn to a non-elected invention. The supplemental IDS filed August 12, 2005 is acknowledged and has been considered. A copy of the PTO-1449 is attached to this Office action.

### *Claim Rejections - 35 USC § 102/103*

2. The following rejections are maintained for reasons of record:

- Claims 1-5, 7, 9-13, 15-18, 21, 37-42, 44-46, 49, 50 and 52-54 remain rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Reimann *et al.* (*Clinical and Diagnostic Laboratory Immunology*, 2000, 7(3):352-359, herein, "Reimann").
- Claims 14 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reimann as applied to claims 1-7, 9-13, 15-18, 21, 37-42, 44-46, 49, 50 and 52-54 above, and further in view of Wisniewski (US Patent 6,337,205).
- Claims 1-31 and 37-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Witt *et al.* (*Journal of Virological Methods*, 1987, 17:287-292, herein, "Witt") in view of Freshney (*Cryopreservation*, Chapter 19, Culture of Animal Cells: a manual of basic technique, 4th edition, Wiley-Liss, 2000, pages 297-308), Invitrogen™'s *Guide to Baculovirus Expression Vector Systems and Insect Cell Culture Techniques*, Kistner *et al.* (*Vaccine*, 1998, 16(9/10):960-968, herein, "Kistner"), Clontech

Laboratories, Inc. document (Protocol #PT3494-2, Version #PR19432, published in 2001, 2 pages, available at http://www.clontech.com) and Nienhuis (US Patent 5,780,447).

The claims as amended are drawn to a cryogenically protected viral delivery system for infecting host cells comprising a cryogenic vessel and a plurality of virally infected cells in admixture with a cryo-protective agent contained in the cryogenic vessel. The concentration of the virally infected cells is from 106 cells/ml to 109 cells/ml; wherein the admixture of the virally infected cells and the cryo-protective agent is at a temperature of less than or equal to –20 C. The viability of the cells contains in the vessel is at least 50%. The new limitation of the claims is that the average cell diameter of cells contained in the cryogenic vessel is at least 0.5 microns greater than the average cell diameter of uninfected cells of the same type.

3. Applicant's arguments have been carefully considered but fail to persuade. Applicant's substantive arguments are primarily drawn to the following:

Applicant argues that Reimann's disclosure is not sufficient to enable the cryopreservation of cells such that the average cell diameter of infected cells is at least 0.5 microns. Specifically, the protocol is directed to the cryopreservation of PBMC cells derived from HIV-1 infected individuals for use in very specific immunotyping and in *in vitro* assay of immune function. The PBMC cells described in Reimann are a heterogenous mixture of cells derived from a diverse population of individuals, making them highly variable in their characterization, and thus very distinct and different from host cells susceptible to infection with a particular virus of interest. Reimann is silent on the type of criteria and specific characteristics

necessary for virally infected cells, such as cell diameter. Without such teachings, one of ordinary skill in the art would not know from Reimann how to carefully select virally infected cells for a cryogenically protected viral delivery system with little loss of the infective potential of the virus, wherein the average cell diameter of infected cells is at least 0.5 microns.

Applicant argues that Reimann's protocol provides no guidance as to the specific characteristics or properties of the admixture, nor of how to deliver infected cells with little loss of the infective potential after preservation. Applicant argues that because Reimann does not assess or observe the particular characteristics in the cell diameter measurements in the admixture, Reimann does not teach the instant invention. Applicant argues that the mere fact that a certain thing may result from a given set of circumstances is not sufficient evidence to support a rejection.

Applicant argues that the claims as amended are not obvious over the prior art. Specifically, none of the references specifically disclose the percent viability of the infected cells, the average cell diameter of cells contained in the cryogenic vessel as being at least 0.5 microns greater than the average cell diameter of uninfected cells of the same type, as well as the admixture being substantially free of extracellular particles, or that the virally infected cells in a vessel are less than or equal to 250 mL. Applicant argues that without the disclosure of the inventors, one would not be able to arrive at the claimed invention.

4. In response to Applicant's arguments, the Office recognizes that Applicant is attempting to overcome the rejections of record by asserting that 1) the claims as amended are not anticipated or obvious over the prior art, and 2) the examiner is using improper hindsight

reconstruction. In response to the second assertion, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the Applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

With regard to the assertion that the newly amended claims are not anticipated or obvious over the prior art, the Office does not consider the new limitation in the independent claims (previously in claim 6, now cancelled) to be adequate to overcome the rejections of record. Regarding the limitation of the virally infected cell diameter being at least 0.5 microns greater than the average cell diameter of uninfected cells of the same type, one would expect that a cell that is infected with viruses would be at least 0.5 microns greater in diameter. Given that more than one virus infected Reimann's PBMCs, and the size of viruses being no larger than 0.3 microns generally, one would expect that the infection of cells with multiple viruses and their progeny would increase the diameter of the infected cell by at least 0.5 microns relative to an uninfected cell. One of ordinary skill in the art would expect that the infected cells of Reimann would, on average, be at least 0.5 microns greater in diameter in comparison to uninfected cells.

Regarding the assertion that the cells of Reimann are heterogeneous to such an extent that they are distinct and different from host cell susceptible to infection with a virus of interest, the Office does not find this argument persuasive. The cells of Reimann fit the description of the claim language. The claims only require that the average cell diameter be assessed, not the

diameter of each cell separately. Applicant is arguing a limitation that is not present in the claims as written.

Regarding the assertion that the references fail to specifically teach that the admixture is substantially free of extracellular viral particles, one would expect that Reimann's protocol removed extracellular viral particles and spent incubation media (EDTA or heparin which the PBMCs were stored in). Nevertheless, "substantially free of extracellular viral particles" is a broad term that lacks definitive endpoints. Given the breath of the term, the prior art meets the claim limitation.

Regarding the assertion that the references fail to teach the percent viability of the cells, Reimann measured viability of the HIV-1infected PBMCs via trypan blue dye exclusion. The viability of the PBMCs prior to freezing was 98%, and the viability post-thawing was 95% (page 352, column 1, Results section, *Specimen donors and PBMC viability*).

In summary, the express, implicit, and inherent disclosures of a prior art reference may be relied upon in the rejection of claims under 35 U.S.C. 102 or 103. "The inherent teaching of a prior art reference, a question of fact, arises both in the context of anticipation and obviousness." In re Napier, 55 F.3d 610, 613, 34 USPQ2d 1782, 1784 (Fed. Cir. 1995) (affirmed a 35 U.S.C. 103 rejection based in part on inherent disclosure in one of the references). See also In re Grasselli, 713 F.2d 731, 739, 218 USPQ 769, 775 (Fed. Cir. 1983). In this case, Applicant has argued that the examiner's conclusion of inherency is improperly based on hindsight, and the absence of consideration of periphery issues (cell heterogeneity of Reimann's PBMCs) would not lead one of ordinary skill in the art to the claimed invention. In response, the teachings of

Reimann are sufficient to meet the limitations of the claims, and are sufficient such that one of ordinary skill in the art would expect Reimann's composition to have the claimed properties.

Therefore, the rejections are maintained for reasons of record.

***Conclusion***

5. No claim is allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James C. Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Stacy B. Chen
January 5, 2006